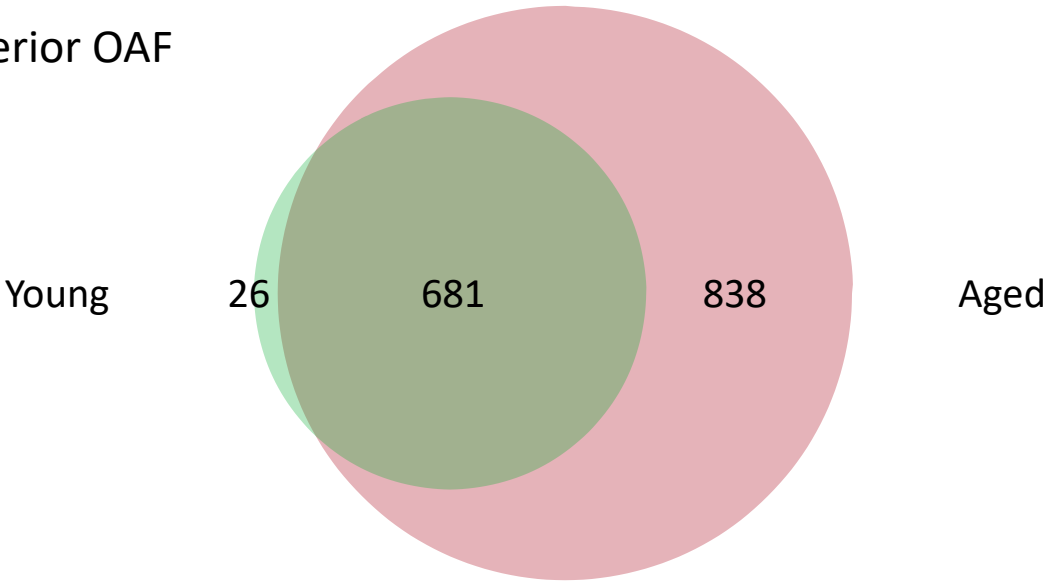
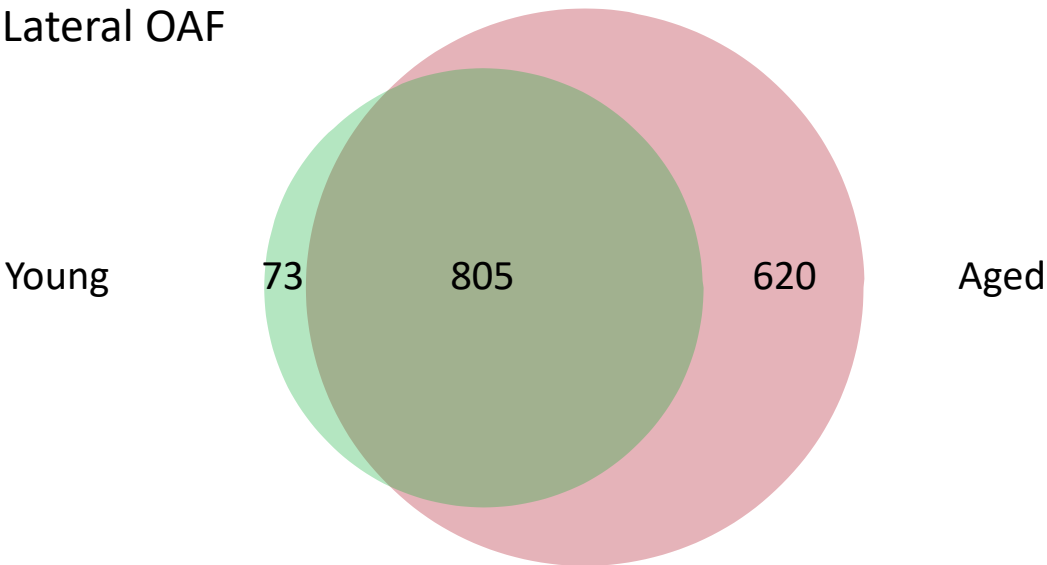


Anterior OAF



Left Lateral OAF



Posterior OAF

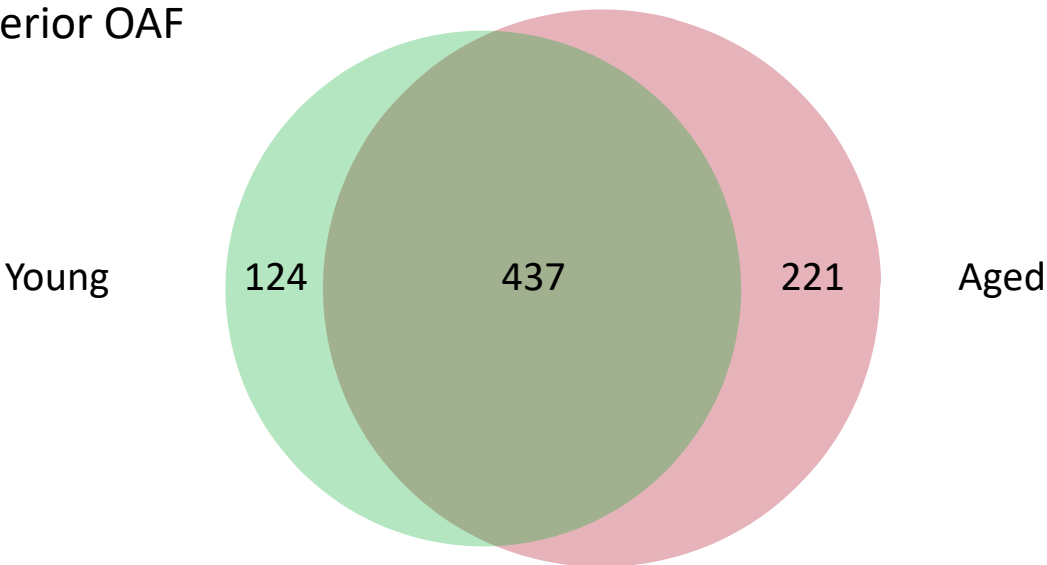
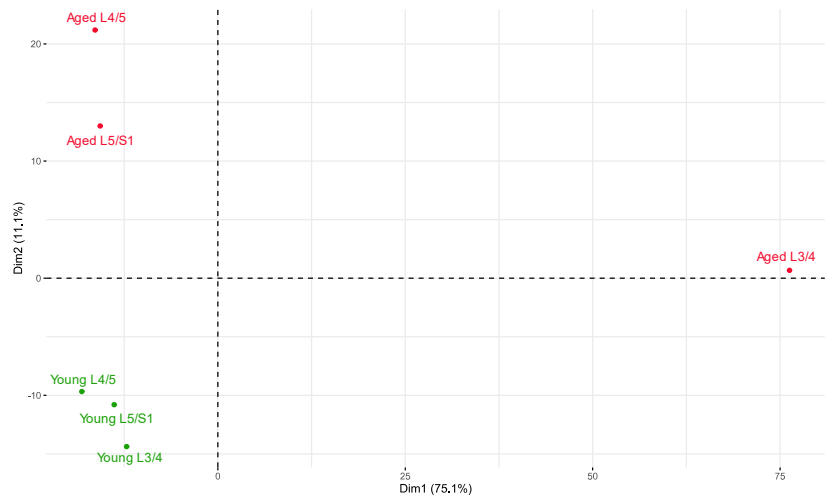
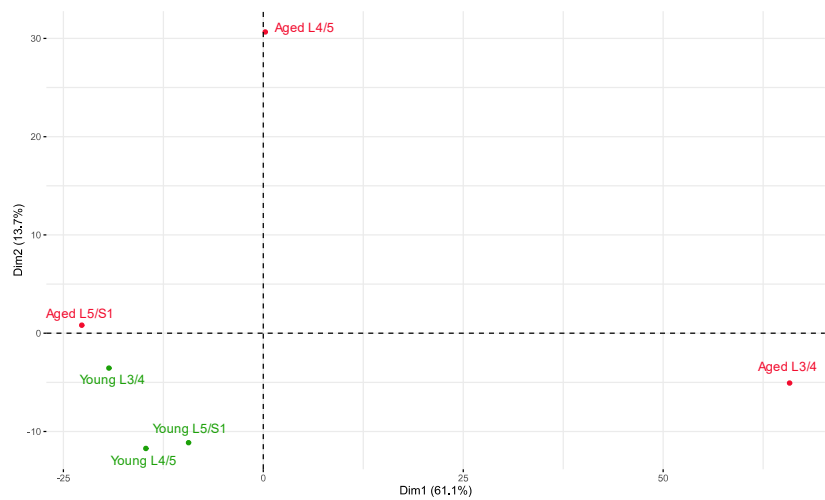


Figure S1. Number of proteins identified by MS/MS ion searches in young and aged samples from each IVD outer AF region.

Anterior



Left Lateral



Posterior

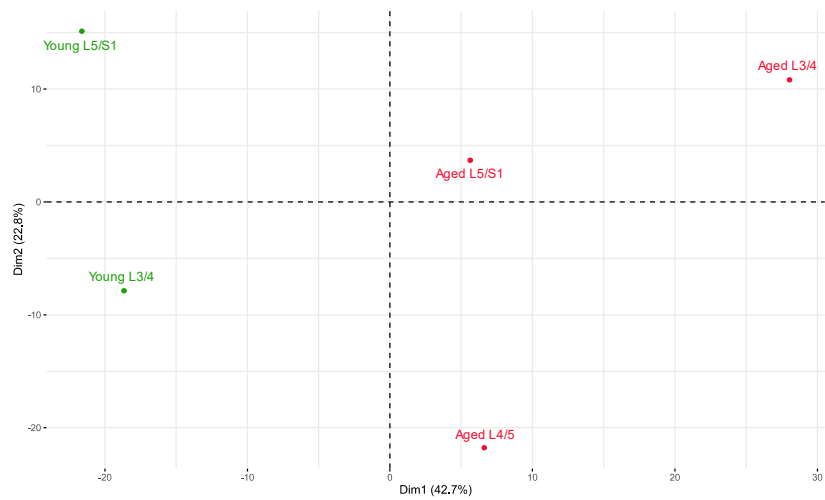


Figure S2. Principal component analyses (performed and visualised using the *FactoMineR* and *factoextra* packages respectively on RStudio) of peptide spectral count data used for peptide location fingerprinting. Aged (red) and young (green) data points show good separation for each IVD region tested.

Shared Biomarker Candidates

ABI3BP, AHNAK, C3, C4A, CCDC80, CILP, CILP2, COL11A2, COL1A2, COL6A1, COL6A3, COL8A1, COMP, CSPG4, FBLN1, FN1, FNDC1, HSPA1A, HSPA1B, HTRA1, LRP1, MATN2, PRG4, TIMP1, TNXB, VCAN

Anterior-only Biomarker Candidates

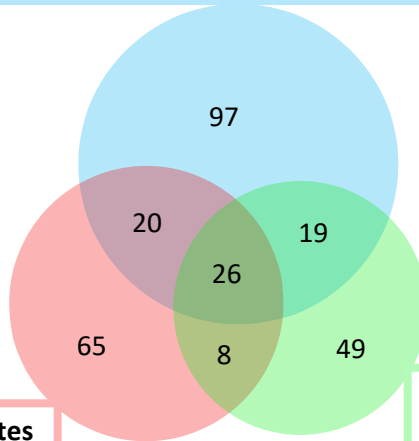
A1BG, ACO2, ACTB, ACTG1, ACTN4, ANGPTL5, ANXA7, APCS, APOA4, APOB, ARF1, ARF3, ARPC4, C1S, C6, CA2, CALD1, CAST, CAVIN1, CAVIN3, CD109, CDH13, CHAD, CHRDL2, COL2A1, COL9A1, COL9A3, CPNE3, CPXM2, CYB5R3, DDOST, DKK3, DPYSL2, ECM1, EEF1G, EMILIN3, ENO3, ENPP2, ERP44, FBLN2, FLNB, FTL, H1-O, H2BC11, H2BC21, H2BC3, HBA1, HBD, HEXA, HHIPL2, HP, IGLC1, ITGB1, ITIH1, KRT1, KRT10, KRT19, LAMB1, LRG1, LTA4H, MRC2, MYH10, MYH11, NACA, NID2, OLFML1, PAM, PDGFC, PDIA6, PEBP1, PFN1, PLG, PRDX2, PRDX4, PRKCSH, PSAP, PSMA7, PYGL, PYGM, RBMX, RPN1, SERPINA1, SERPINA3, SERPINB6, SERPIND1, SERPING1, SET, SNC73, SOD3, SPTAN1, SRPX2, SYNCRIIP, TGM2, THBS2, THBS4, TINAGL1, VASN

Anterior and Left Lateral Shared Biomarker Candidates

COL4A1, COL4A2, COL5A2, COL9A2, DPT, ECM2, FLNA, FRZB, HNRNPU, ISLR, ITIH2, LAMA2, LAMA5, LAMB2, MELTF, MXRA5, OAF, P4HA1, PLEC, SEMA3C

Anterior and Posterior Shared Biomarker Candidates

ATP1A1, C2, CFH, COL11A1, COL14A1, COL15A1, COL5A1, FBN1, FGA, FGB, H4C1, HPX, HSPA8, NUCB2, TIMP3, TNC, TTR, TUBA1B, VTN



Left Lateral-only Biomarker Candidates

ACLY, ACTN3, ARHGDIB, CALU, CCN2, CDH1, CLEC3B, COL1A1, CTGF, CTSG, DAG1, DYNC1H1, ENPP1, FLNC, GAA, GANAB, GAPDH, GBE1, GCS1, GSTP1, H1-5, HIST1H1E, HNRNPH1, HSP90AB1, HTRA3, IDH2, IGFBP3, IGFBP7, IGHM, ITGAV, ITIH4, ITIH6, KRT9, LAMC1, LCP1, LGALS3BP, LOXL3, MAP1B, MDH2, MPO, MYOM2, NEB, NID1, NNMT, PLS3, PRDX3, PRKAR1A, PRTN3, PXYLP1, RACK1, RAP1B, RPN2, S100A9, SCIN, SEMA3E, SERPINA4, SLC4A1, SPARC, SPTA1, SRI, THBS1, TPM1, TUBB2C, TUBB4B, VWA1

Left Lateral and Posterior Shared Biomarker Candidates

ACAN, CLTC, F2, FHL1, GC, LTBP2, PPIC, UGDH

Posterior-only Biomarker Candidates

A2M, AMBP, ANGPTL2, ANXA2, ANXA5, APOE, BGN, CALM1, CALM2, CALM3, CAPS, CKM, CLEC3A, COL6A2, CRYAB, DRIP4, EEF1A1, EEF1A1P5, F13A1, FBXO2, FSCN1, GDI2, GLUD1, GSN, HEL-214, HRG, HSPA5, HSPG2, IGK@, KNG1, MSN, NCL, NUCB1, ORM2, PCOLCE2, PDCD6IP, PGD, PLOD1, PTRF, SERPINE1, SMOC1, SMOC2, STRF8, TALDO1, TF, THBS3, TUBA1A, TUBB, TXNDC5

Figure S3. Shortlisted protein targets of IVD OAF ageing identified with structure-associated differences by peptide location fingerprinting (PLF). PLF identified 284 proteins across the three tissue regions tested, 26 of which were shared between all regions.

Age-affected IVD OAF proteins identified with structural modifications by PLF

Extracellular Matrix (43)

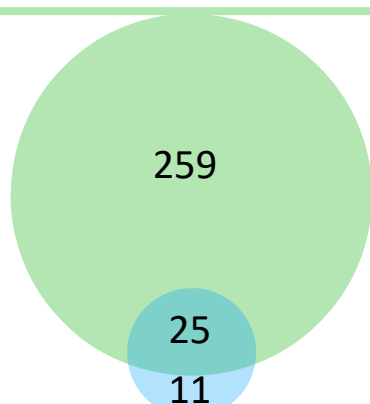
Structural - COL11A1, COL14A1, COL2A1, COL4A1, COL4A2, COL5A1, COL8A1, COL9A1, COL9A2, COL9A3

Associated - AMBP, CILP, CILP2, COMP, DAG1, DPT, ECM1, ECM2, EMILIN3, FBLN1, FBLN2, FN1, FNDC1, LAMA2, LAMA5, LAMB1, LAMB2, LAMC1, LOXL3, LTBP2, MATN2, NID1, NID2, PCOLCE2, THBS1, THBS2, THBS3, THBS4, TNC, TNXB

Proteoglycan - ACAN, CSPG4, PRG4

Other Proteins (216)

A1BG, A2M, ACLY, ACO2, ACTB, ACTG1, ACTN3, ACTN4, AHNK, ANGPTL2, ANGPTL5, ANXA2, ANXA7, APOB, ARF1, ARF3, ARHGDIB, ARPC4, ATP1A1, C1S, C2, C3, C4A, CA2, CALD1, CALM1, CALM2, CALM3, CALU, CAPS, CAST, CAVIN1, CAVIN3, CCDC80, CCN2, CD109, CDH1, CDH13, CFH, CHAD, CHRDL2, CKM, CLEC3A, CLEC3B, CLTC, CPNE3, CPXM2, CRYAB, CTGF, CTSG, CYB5R3, DDOST, DKK3, DPYSL2, DRIP4, DYNC1H1, EEF1A1, EEF1A1P5, EEF1G, ENO3, ENPP1, ENPP2, ERP44, F2, FBOXO2, FGA, FGB, FHL1, FLNA, FLNB, FLNC, FRZB, FSCN1, FTL, GAA, GANAB, GAPDH, GBE1, GC, GCS1, GDI2, GLUD1, GSN, GSTP1, H1-0, H1-5, H2BC11, H2BC21, H2BC3, H4C1, HBA1, HBD, HEL-214, HEXA, HHIPL2, HIST1H1E, HNRNPH1, HNRNPU, HP, HPX, HRG, HSP90AB1, HSPA1A, HSPA1B, HSPA5, HSPA8, HTRA1, HTRA3, IDH2, IGFBP3, IGFBP7, IGK@, IGLC1, ISLR, ITGAV, ITGB1, ITIH1, ITIH2, ITIH6, KNG1, KRT1, KRT10, KRT19, KRT9, LCP1, LGALS3BP, LRG1, LRP1, LTA4H, MAP1B, MDH2, MELTF, MPO, MRC2, MSN, MXRA5, MYH10, MYH11, MYOM2, NACA, NCL, NEB, NNMT, NUCB1, NUCB2, OAF, OLFML1, ORM2, P4HA1, PAM, PDCD6IP, PDGFC, PDIA6, PEBP1, PFN1, PGD, PLEC, PLOD1, PLS3, PPIC, PRDX2, PRDX3, PRDX4, PRKAR1A, PRKCSH, PRTN3, PSAP, PSMA7, PTRF, PXYLP1, PYGL, PYGM, RACK1, RAP1B, RBMX, RPN1, RPN2, S100A9, SCIN, SEMA3C, SEMA3E, SERPINA1, SERPINA3, SERPINA4, SERPINB6, SERPIND1, SERPINE1, SERPING1, SET, SLC4A1, SMOC1, SMOC2, SNC73, SOD3, SPTA1, SPTAN1, SRI, SRPX2, STRF8, SYNCRIIP, TALDO1, TF, TGM2, TIMP1, TIMP3, TINAGL1, TPM1, TTR, TUBA1A, TUBA1B, TUBB, TUBB2C, TUBB4B, TXNDC5, UGDH, VASN



Age-affected IVD OAF proteins identified with differences in relative abundance (LFQ) and structural modifications (PLF)

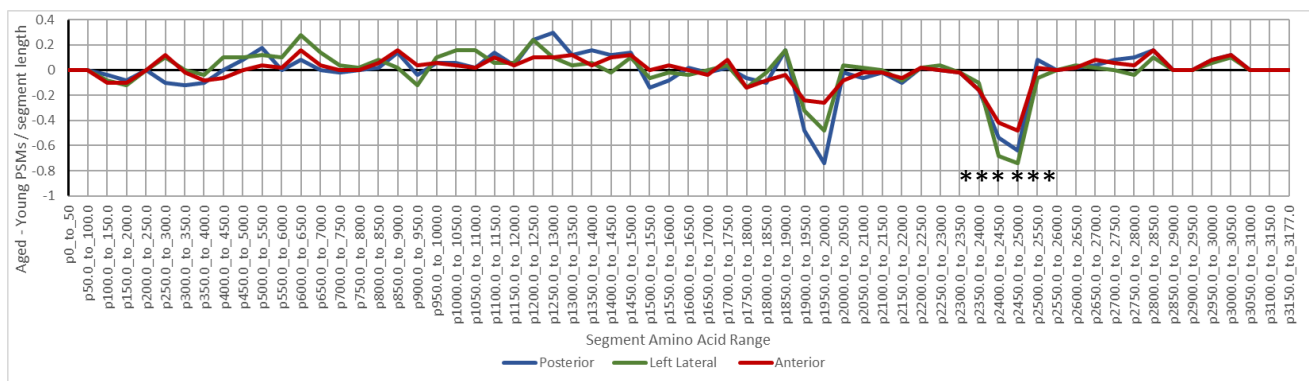
ABI3BP, ANXA5, APCS, APOA4, APOE, BGN, C6, COL11A2, COL15A1, COL1A1, COL1A2, COL5A2, COL6A1, COL6A2, COL6A3, F13A1, FBN1, HSPG2, IGHM, ITIH4, PLG, SPARC, VCAN, VTN, VWA1

Age-affected IVD OAF proteins identified with differences in whole protein relative abundance by LFQ

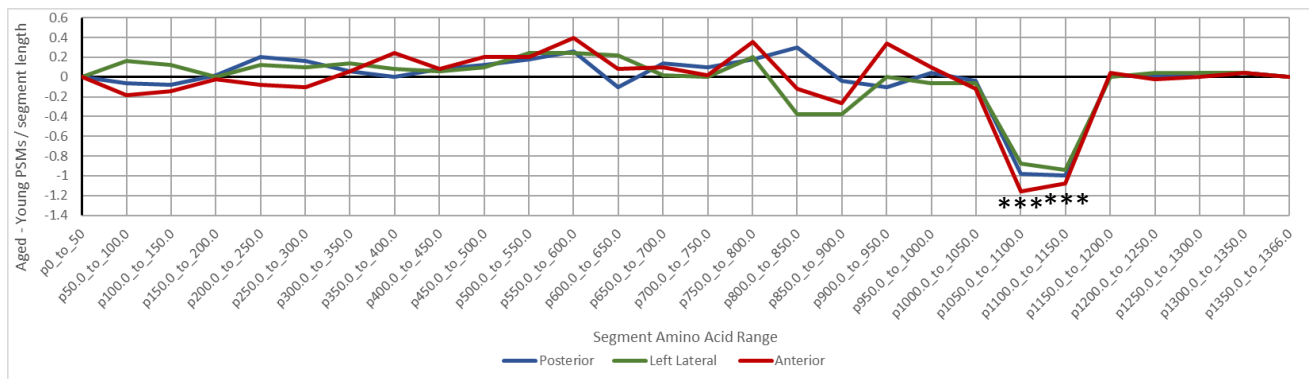
AHSG, ANXA1, ANXA4, APOH, C9, CTSD, HAPLN3, IL17B, LOX, MMP2, POSTN

Figure S4. Protein targets of IVD OAF ageing identified in the original Tam *et al.* (2020) study by label-free quantification (LFQ) of relative protein abundance and in this study by peptide location fingerprinting (PLF). PLF identified 259 proteins that were potentially unique to the approach, with age-associated significant differences in protein structure but not abundance.

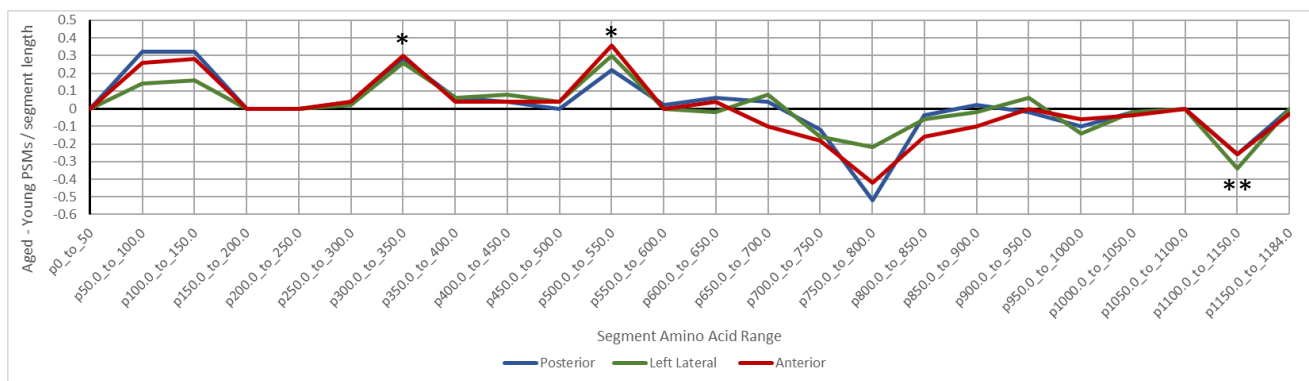
Collagen alpha-3(VI) chain (COL6A3)



Collagen alpha-2(I) chain (COL1A2)



Cartilage intermediate layer protein 1 (CILP1)



Cartilage intermediate layer protein 2 (CILP2)

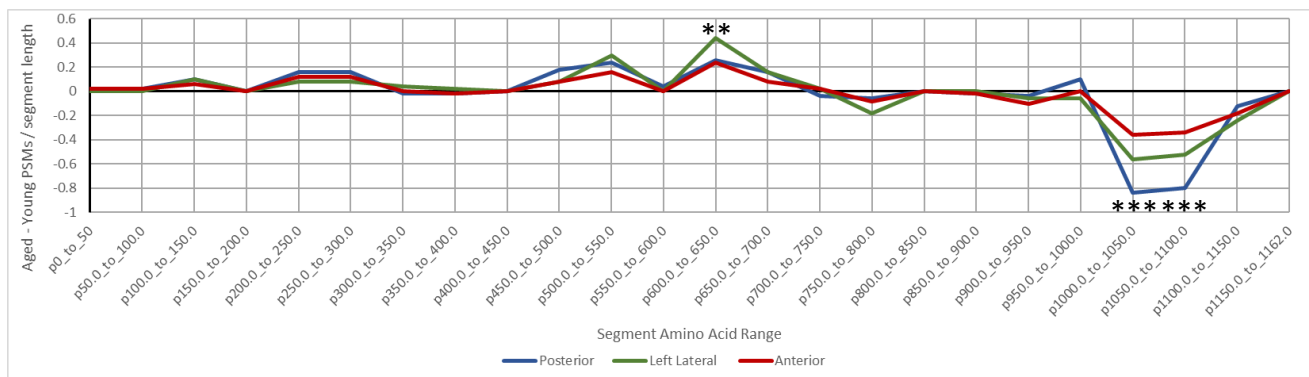
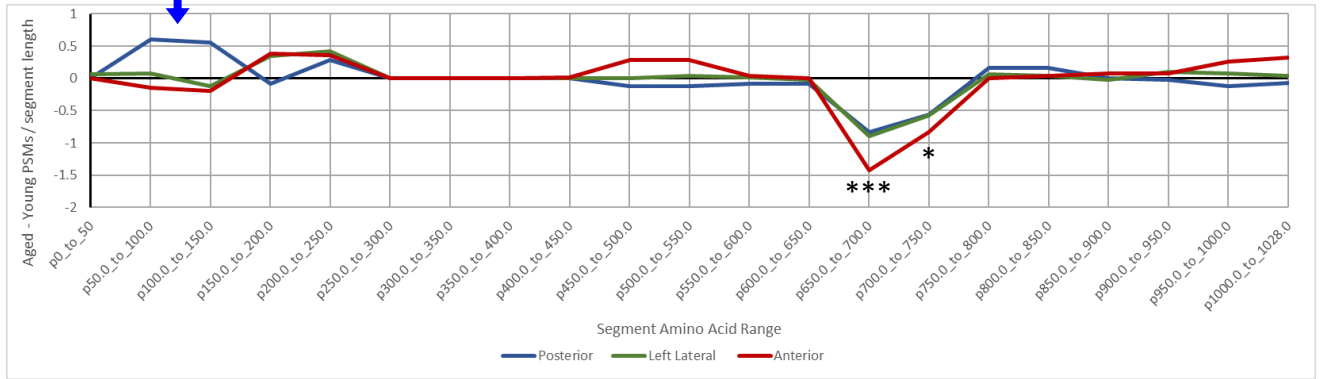
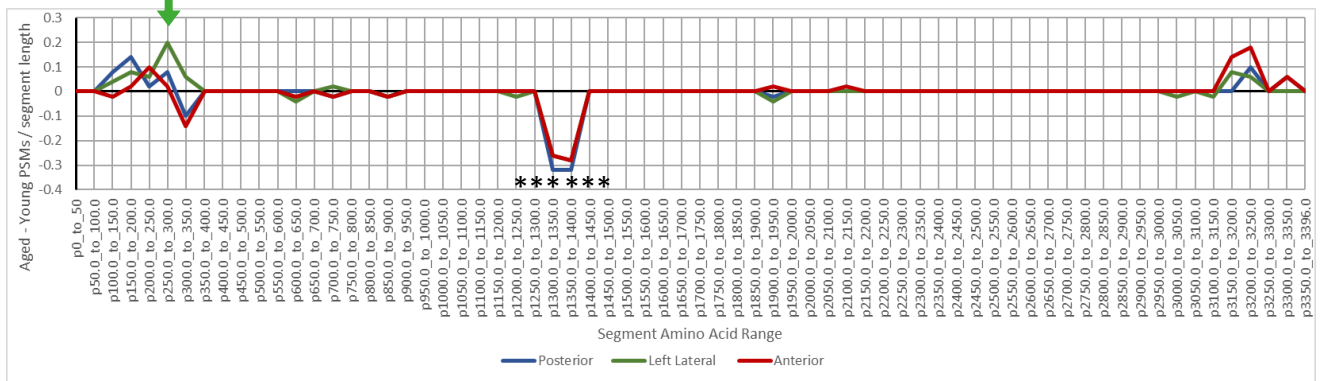


Figure S5. Non-normalised representations of composite lines graphs (**Fig. 3**) of ECM proteins displaying tissue region-conserved, significant differences in peptide yield across their segmented structures between young and aged IVD OAF ($y = 0$ indicates either no difference between young and aged or missing values in both groups; stats = unpaired Bonferroni-corrected, repeated measures ANOVAs: *, $p \leq 0.05$; **, $p \leq 0.01$; ***, $p \leq 0.001$; stars = significant in all three tissue regions)

Collagen alpha-1(VI) chain (COL6A1)



Versican core protein (VCAN)



Complement C3 (C3)

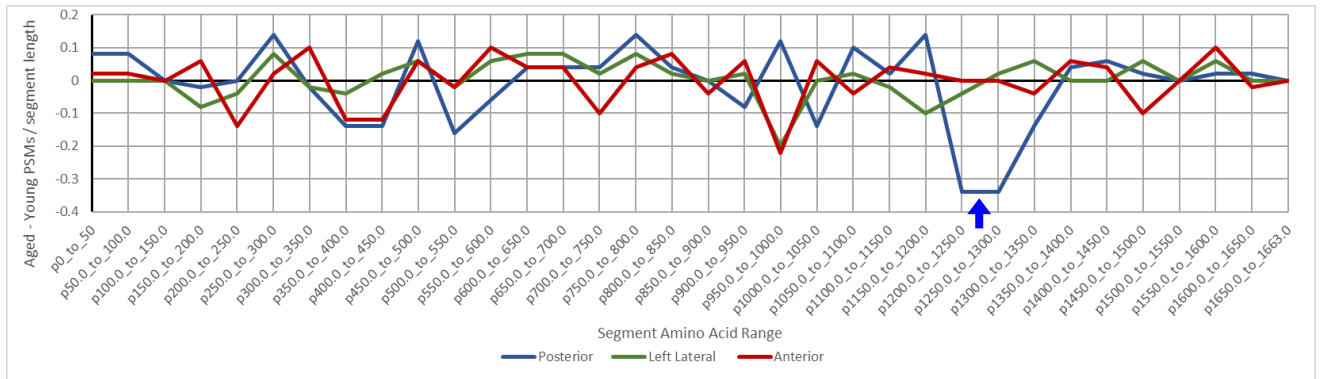


Figure S6. Non-normalised representations of composite lines graphs (**Fig. 4**) of proteins displaying both tissue region-conserved and -specific, significant differences in peptide yield across their segmented structures between young and aged IVD OAF ($y = 0$ indicates either no difference between young and aged or missing values in both groups; stats = unpaired Bonferroni-corrected, repeated measures ANOVAs: *, $p \leq 0.05$; **, $p \leq 0.01$; ***, $p \leq 0.001$; stars = significant in all three tissue regions; coloured arrows = significant, tissue region-specific differences)

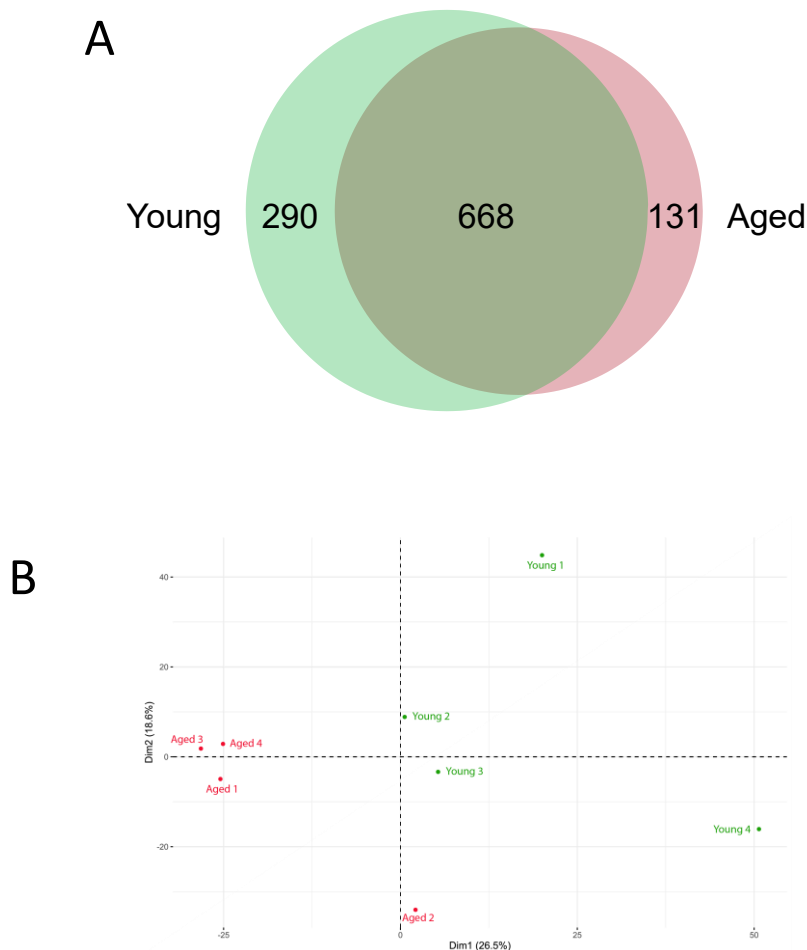


Figure S7. Number of proteins identified by MS/MS ion searches in young and aged mouse lung samples **(A)**. Principal component analysis (performed and visualised using the *FactoMineR* and *factoextra* packages respectively on RStudio) of peptide spectral count data used for peptide location fingerprinting **(B)**. Aged (red) and young (green) data points show good data separation.

Age-affected mouse lung proteins identified with structural modifications by PLF

Extracellular Matrix (26)

Structural – Col15a1, Col1a1, Col4a2, Col4a5, Col6a2, Eln, Fbn1

Associated - Ecm1, Efemp1, Fbln5, Fn1, Lama1, Lama2, Lama3, Lama4, Lama5, Lamb1, Lamb2, Lamc1, Lamc2, Mmrn1, Postn, Tgfb1, Vwf

Proteoglycan - Dag1, Hspg2

Other Proteins (108)

Abi3bp, Aco2, Actr2, Add1, Ahnak, Alb, Ap2a2, Apoa1, Arhgef7, Arpc1b, Atp1a1, Atp5f1b, C4b, Cavin1, Ccdc170, Ccdc187, Cep135, Ces1d, Cfh, Coro1c, Cp, Crocc2, Ddx5, Dhx9, Dpep1, Dsp, Dstn, Dync1h1, Ehd4, Emid1, Eppk1, Ezr, Fermt2, Fga, Fgb, Flii, Flna, Gdi2, H1-2, Hadhb, Hmcn1, Hnrnpl, Hpgd, Hspa12b, Hspa5, Igfbp7, Itga8, Khdrbs1, Kpnb1, Krt1, Lsp1, Macf1, Macroh2a1, Mlf1, Mprp, Myh10, Myh2, Myh7, Myh8, Myl6, Mylk, Myo18a, Myo1c, Myom2, Ncl, Pakap, Parp1, Pdcd6ip, Pdia3, Pi15, Plcb3, Poc5, Ppia, Ppp1cc, Ppp2r1a, Prx, Pxdn, Rac1, Rpl14, Rpl7a, Ruvbl1, Samhd1, Sec31a, Sema3e, Serpina1b, Serpina1d, Serpina3k, Serpinc1, Serpinh1, Slc25a4, Smc3, Sorbs1, Spata6, Sptan1, Sqor, Stab1, Slep1, Syne1, Tgm2, Tinagl1, Tjp1, Tns3, Top2b, Tpm1, Ttn, Tubb5, Txndc5, Wdr1

134

5

197

Age-affected mouse lung proteins identified with differences in relative abundance (LFQ) and structural modifications (PLF)

Agrn, Cma1, Col4a3, Ighg2b, Myo1b, Vtn

Age-affected mouse lung proteins identified with differences in whole protein relative abundance by LFQ

A1bg, Aacs, Acox1, Adamtsl4, Adcy9, Adhfe1, Adss, Akip1, Akna, Aktip, Alms1, Ambp, Arf2, Arhgap18, Arhgap35, Arl6ip6, Atp7b, Atp8, Bbs7, Bckdha, Borcs7, Bpifa1, Bpifb1, C1qc, C1qtnf5, C6, C7, C8a, C8b, C8g, C9, Ca3, Camsap3, Ccdc57, Ccdc58, Ccdc77, Ccnk, Cd55, Cdk11b, Cfhr2, Cfi, Chd3, Cilp, Cilp2, Ciz1, Cmya5, Cntl, Col14a1, Col16a1, Col6a4, Col6a5, Col6a6, Commd8, Creg1, Ctdsp1, Cwc15, Cxcl12, Dhtkd1, Dlgap4, Dmd, Dpp8, Dtymk, Ebna1bp2, Ecsr, Ehbp1, Enpp5, Erc2, Eva1b, F13b, Fbxo18, Fetub, Fhl2, Flt1, Fmod, Fras1, Frem1, Frem2, Get4, Gimap7, Glt28d2, Gm12250, Gm15800, Gm4788, Gmeb1, Gpx7, Gtf3c2, Gtf3c5, Gypc, H2Eb, Hars2, Hbb-y, Hp, Hpx, Hydin, Hypk, Ift81, Ift88, IgG1TS1VH, Igh, Ighm, Ighvdj, Igkv10-96, Igv3, Ikzf3, Impad1, Irak4, Isoc2a, Itfg1, Itgb4, Itih3, Krt10, Krt2, Krt6a, Lox, Lrg1, Ltbp2, Ly6a, Mcpt8, Mfap5, Mfge8, Mgl2, Mgp, Minos1, Mpz, Mtmr12, Mug1, Myl2, Naa40, Naalad2, Nbeal1, Ndst1, Neb1, Nefh, Nefl, Nefm, Nelfe, Nfia Nnt, Nsdhl, Orm1, P2rx7, Pbx1, Pclo, Pet100, Pex5l, Phf14, Pi4k2a, Pih1d1, Plekhf2, Plin1, Pmfbp1, Ppp1r11, Prdm16, Prph, Prss34, Psmb10, Ptpz1, Rabggt, Rad50, Rasal2, Rcn3, Rfx1, Rpap3, Sacs, Sap130, Sash3, Sdc4, Sdcbp, Sema7a, Sept1, Serpina1e, Serpinb9b, Slc14a1, Slc27a4, Smc6, Smdt1, Snip1, Spata5, Spcs3, Ston2, Tbc1d31, Tcea3, Tm9sf4, Tmem261, Tor4a, Tox4, Tpm2, Tsc2, Tspan18, Ube2g2, Ubfd1, Upk3b, Vamp2, Wdfy1, Wnt9a, Yipf6, Znf532

Figure S8. Protein targets of mouse lung ageing identified in the original Angelidis and Simon *et al.* (2019) study by label-free quantification (LFQ) of relative protein abundance and in this study by peptide location fingerprinting (PLF). PLF identified 134 proteins that were potentially unique to the approach, with age-associated significant differences in protein structure but not abundance.

Shared Biomarker Candidates between Human IVD and Mouse Lung Ageing

ABI3BP, ACO2, AHNK, ATP1A1, CAVIN1, CFH, COL15A1, COL1A1, COL4A2, COL6A2, DAG1, DYNC1H1, ECM1, FBN1, FGA, FGB, FLNA, FN1, GDI2, HSPA5, HSPG2, IGFBP7, KRT1, LAMA2, LAMA5, LAMB1, LAMB2, LAMC1, MYH10, MYOM2, NCL, PDCD6IP, SEMA3E, SPTAN1, TGM2, TINAGL1, TPM1, TXNDC5, VTN

Human IVD

245

39

101

Mouse Lung

Ageing Human IVD-only Biomarker Candidates

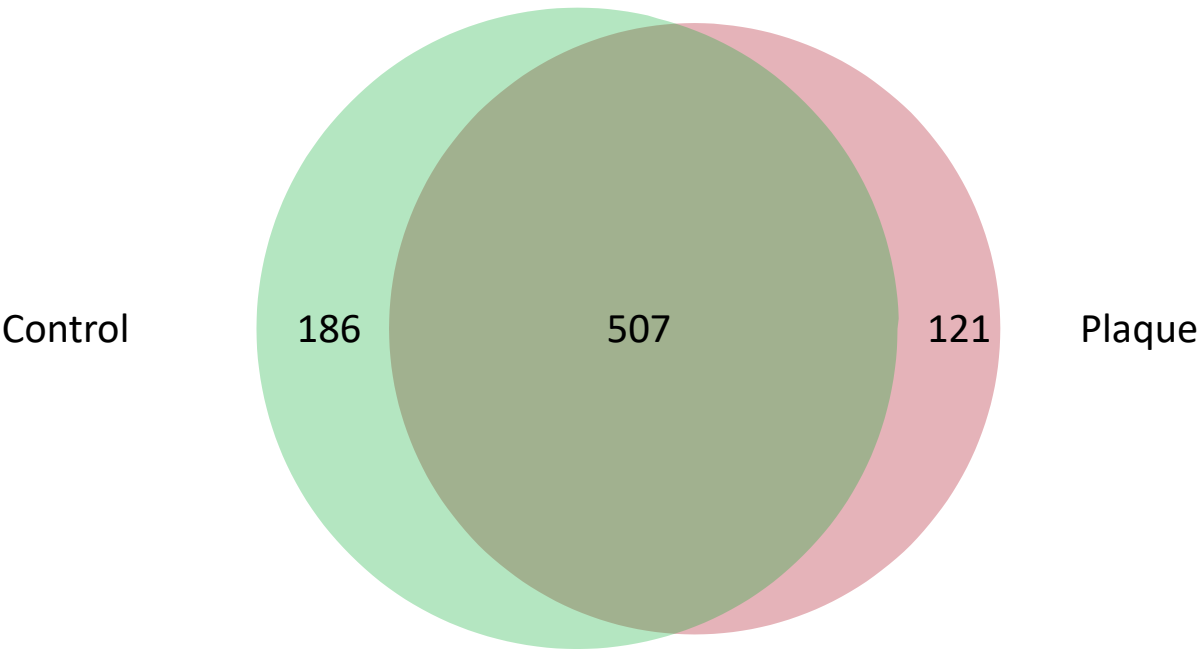
A1BG, A2M, ACAN, ACLY, ACTB, ACTG1, ACTN3, ACTN4, AMBP, ANGPTL2, ANGPTL5, ANXA2, ANXA5, ANXA7, APCS, APOA4, APOB, APOE, ARF1, ARF3, ARHGDIB, ARPC4, BGN, C1S, C2, C3, C4A, C6, CA2, CALD1, CALM1, CALM2, CALM3, CALU, CAPS, CAST, CAVIN3, CCDC80, CCN2, CD109, CDH1, CDH13, CHAD, CHRD12, CILP, CILP2, CKM, CLEC3A, CLEC3B, CLTC, COL11A1, COL11A2, COL14A1, COL1A2, COL2A1, COL4A1, COL5A1, COL5A2, COL6A1, COL6A3, COL8A1, COL9A1, COL9A2, COL9A3, COMP, CPNE3, CPXM2, CRYAB, CSPG4, CTGF, CTSG, CYB5R3, DDOST, DKK3, DPT, DPYSL2, DRIP4, ECM2, EEF1A1, EEF1A1P5, EEF1G, EMILIN3, ENO3, ENPP1, ENPP2, ERP44, F13A1, F2, FBLN1, FBLN2, FBXO2, FHL1, FLNB, FLNC, FNDC1, FRZB, FSCN1, FTL, GAA, GANAB, GAPDH, GBE1, GC, GCS1, GLUD1, GSN, GSTP1, H1-0, H1-5, H2BC11, H2BC21, H2BC3, H4C1, HBA1, HBD, HEL-214, HEXA, HHIPL2, HIST1H1E, HNRNPH1, HNRNPU, HP, HPX, HRG, HSP90AB1, HSPA1A, HSPA1B, HSPA8, HTRA1, HTRA3, IDH2, IGFBP3, IGHM, IGK@, IGLC1, ISLR, ITGAV, ITGB1, ITIH1, ITIH2, ITIH4, ITIH6, KNG1, KRT10, KRT19, KRT9, LCP1, LGALS3BP, LOXL3, LRG1, LRP1, LTA4H, LTBP2, MAP1B, MATN2, MDH2, MELTF, MPO, MRC2, MSN, MXRA5, MYH11, NACA, NEB, NID1, NID2, NNMT, NUCB1, NUCB2, OAF, OLFML1, ORM2, P4HA1, PAM, PCOLCE2, PDGFC, PDIA6, PEBP1, PFN1, PGD, PLEC, PLG, PLOD1, PLS3, PPIC, PRDX2, PRDX3, PRDX4, PRG4, PRKAR1A, PRKCSH, PRTN3, PSAP, PSMA7, PTRF, PXYLP1, PYGL, PYGM, RACK1, RAP1B, RBMX, RPN1, RPN2, S100A9, SCIN, SEMA3C, SERPINA1, SERPINA3, SERPINA4, SERPINB6, SERPIND1, SERPINE1, SERPING1, SET, SLC4A1, SMOC1, SMOC2, SNC73, SOD3, SPARC, SPTA1, SRI, SRPX2, STRF8, SYNCRIIP, TALDO1, TF, THBS1, THBS2, THBS3, THBS4, TIMP1, TIMP3, TNC, TNXB, TTR, TUBA1A, TUBA1B, TUBB, TUBB2C, TUBB4B, UGDH, VASN, VCAN, VWA1

Ageing Mouse Lung-only Biomarker Candidates

Actr2, Add1, Agrn, Alb, Ap2a2, Apoa1, Arhgef7, Arpc1b, Atp5f1b, C4b, Ccdc170, Ccdc187, Cep135, Ces1d, Cma1, Col4a3, Col4a5, Coro1c, Cp, Crocc2, Ddx5, Dhx9, Dpep1, Dsp, Dstn, Efemp1, Ehd4, Eln, Emid1, Eppk1, Ezr, Fbln5, Fermt2, Flii, H1-2, Hadhb, Hmcn1, Hnrnpl, Hpgd, Hspa12b, Ighg2b, Itga8, Khdrbs1, Kpn1b, Lama1, Lama3, Lama4, Lamc2, Lsp1, Macf1, Macroh2a1, Mlf1, Mmrn1, Mrip, Myh2, Myh7, Myh8, Myl6, Mylk, Myo18a, Myo1b, Myo1c, Pakap, Parp1, Pdia3, Pi15, Plcb3, Poc5, Postn, Ppia, Ppp1cc, Ppp2r1a, Prx, Pxdn, Rac1, Rpl14, Rpl7a, Ruvbl1, Samhd1, Sec31a, Serpina1b, Serpina1d, Serpina3k, Serpinc1, Serpinh1, Slc25a4, Smc3, Sorbs1, Spata6, Sqor, Stab1, Svp1, Syne1, Tgfbi, Tjp1, Tns3, Top2b, Ttn, Tubb5, Vwf, Wdr1

Figure S9. Shortlisted protein targets of human IVD and mouse lung ageing identified with structure-associated differences by peptide location fingerprinting (PLF). PLF identified 39 proteins which were age-affected in both human and mouse.

Male



Female

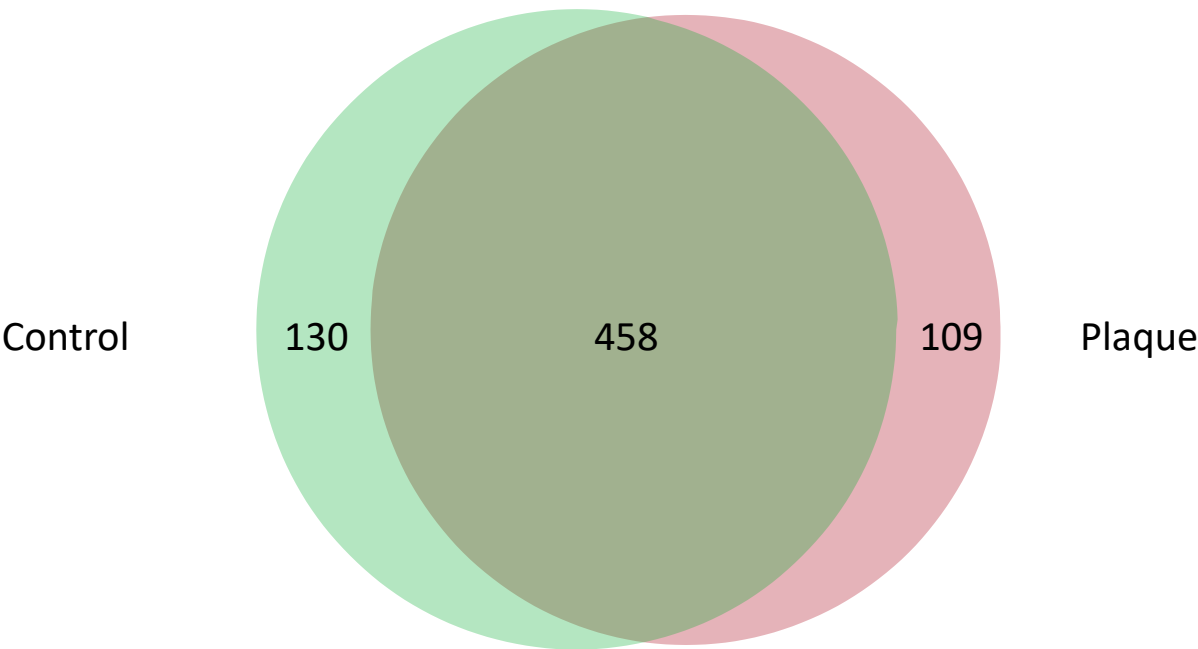
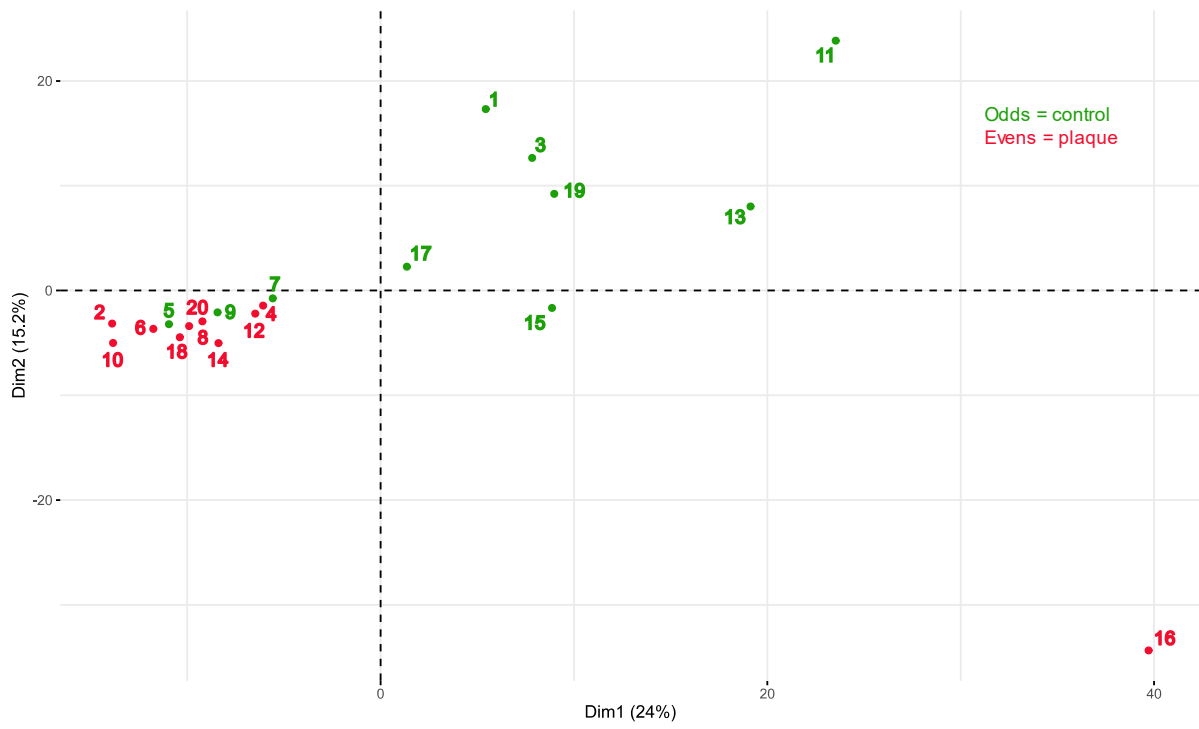


Figure S10. Number of proteins identified by MS/MS ion searches in plaque and control samples from male and female atherosclerotic artery.

Male



Female

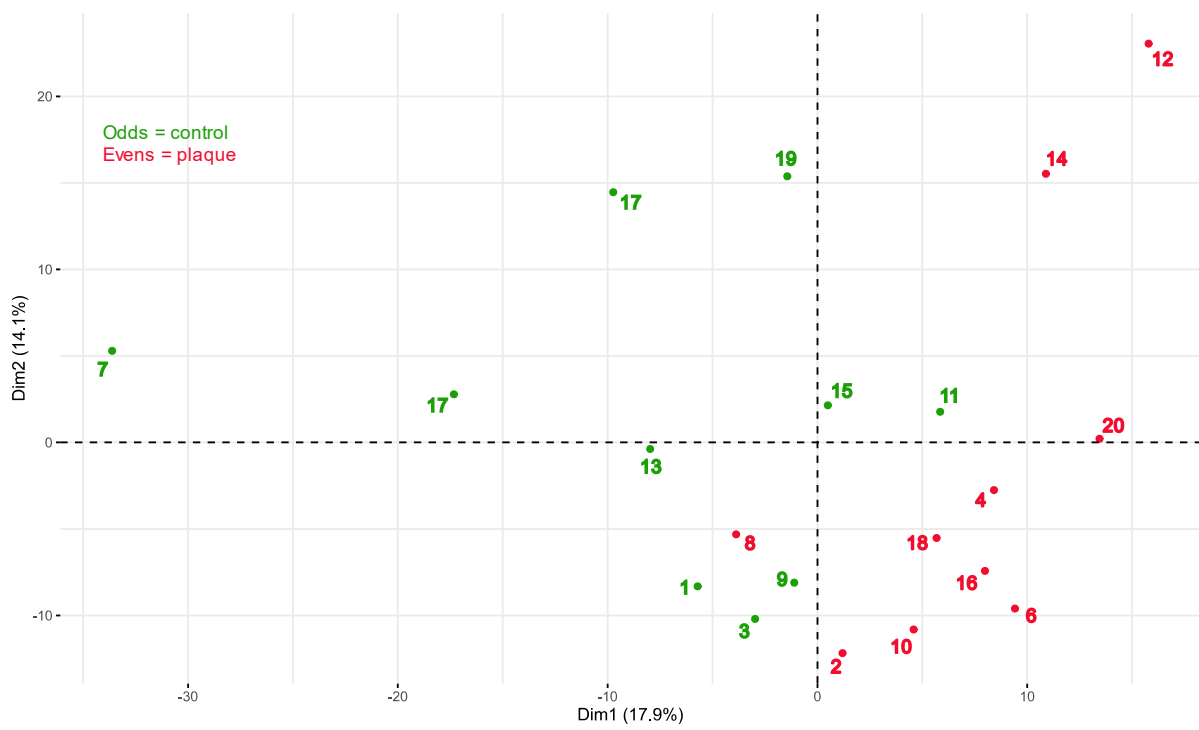
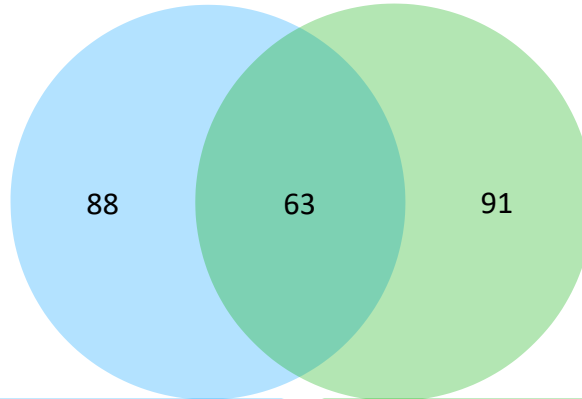


Figure S11. Principal component analyses (performed and visualised using the *FactoMineR* and *factoextra* packages respectively on RStudio) of peptide spectral count data used for peptide location fingerprinting. Plaque (red/even) and control (green/odd) data points show good separation for both male and female samples.

Shared Biomarker Candidates

ACTC1, ACTN4, AHNAK, ANK1, APOB, APOL1, APOM, AQP1, C4A, C4BPB, C7, CAVIN1, CDH13, CFI, COL12A1, COL18A1, COL1A2, COL4A1, COL4A2, COL5A1, COL8A2, CTSB, DPYSL3, EEF2, F2, FBLN1, FCN3, FERMT3, FHL1, FLNA, GPNMB, GSTO1, H4C1, HSPG2, IQGAP1, ITGB2, LAMC1, LAMP1, LASP1, LBP, LRP1, LTF, MYH11, MYH9, OGN, PFN1, PLEC, PLS3, PRDX2, RTN4, SERPIND1, SERPINF1, SOD3, SPTA1, SPTB, TF, THBS1, TIMP1, TLN1, TNC, TPM3, TPP1, YWHAG



Female-only Biomarker Candidates

A2M, ACTR2, ACTR3, AEBP1, AFM, AMBP, ANXA1, AOC3, APOA1, APOD, APOE, ATP6V1A, C1QA, C1QB, C2, C3, C6, C8B, CD36, CFHR1, CFL1, CLIC1, CNDP2, CNN1, COL1A1, COL3A1, COL6A1, CORO1A, CP, CPN2, CRIP2, CSRP1, CYB5R3, DEFA1, DEFA3, EFEMP1, EIF4A1, EMILIN2, F10, F13A1, FBLN5, FGG, FN1, GAS6, GNAI2, H3-3A, H3F3B, HPR, IGA2HC, IGFALS, IGHG3, ITGB1, KRT1, LTBP1, LTBP2, MMP12, MYH10, MYL12A, NID1, PDIA3, PGD, PGK1, PLD3, PLTP, PON1, POSTN, PRDX6, PROS1, PZP, RAP1B, S100A11, S100A6, SAA4, SERPINA1, SERPINA10, SERPINA3, SERPINE2, SERPINF2, SERPING1, SPP2, TALDO1, TKT, TNXB, UBA52, VCAN, VCP, VTN, YWHAZ

Male-only Biomarker Candidates

ACTB, ACTG1, ALB, ALDH2, ANPEP, APOA4, ARPC3, ASAH1, ATP5F1B, C1R, C8G, CALD1, CALR, CANX, CAPG, CAPZB, CAST, CCT5, CLEC3B, CLU, CNN3, COL14A1, COL6A2, CSPG2, CTSZ, DPYSL2, DSTN, EEF1A1, EMILIN1, FBLN2, FMOD, FTH1, GDI2, GNB1, GPI, H3C15, HBB, HCLS1, HNRNPA2B1, HNRNPD, HNRNPK, HP, HSP90AB1, HSP90B1, HSPA9, IGGLC, IGH@, IGK, IGL@, ILK, KCTD12, KLKB1, KRT10, KRT9, LDHB, LPA, MARCKS, MMP9, MPO, NPM1, ORM2, PDIA4, PDIA6, PDLIM3, PGAM1, PGLYRP2, PLG, PPIB, PRKCSH, RPLP2, S100A8, SAA1, SAMHD1, scFv, SEPTIN7, SERBP1, SERPINA4, SERPINH1, SH3BGRL3, SLC2A1, SLC4A1, SOD1, SPTAN1, STOM, TGM2, TPI1, TUBB4B, VCL, WDR1, YWHAH, YWHAQ

Figure S12. Shortlisted protein targets of arterial atherosclerosis identified with structure-associated differences by peptide location fingerprinting (PLF). PLF identified 242 proteins across both sexes, 63 of which were shared between females and males.

Atherosclerosis proteins identified with structural modifications by PLF

Extracellular Matrix (16)

Structural - COL12A1, COL14A1, COL1A1, COL1A2, COL3A1, COL4A2, COL5A1, COL6A1, COL6A2, COL8A2

Associated - AMBP, EMILIN2, FN1, THBS1, TNC

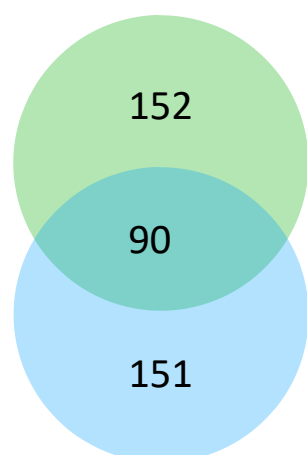
Proteoglycan - VCAN

Other Proteins (136)

ACTB, ACTC1, ACTR2, ACTR3, AEBP1, AFM, AHNAK, ALB, ALDH2, ANK1, ANPEP, ANXA1, ARPC3, ASAH1, ATP5F1B, ATP6V1A, C1QA, C1QB, C1R, C2, C7, CALR, CANX, CAPG, CAPZB, CAST, CCT5, CD36, CFHR1, CFI, CFL1, CLEC3B, CLU, CNDP2, CORO1A, CPN2, CSPG2, CSRP1, CTSZ, DEFA1, DPYSL2, DPYSL3, DSTN, EEF1A1, EEF2, EIF4A1, F10, F13A1, GAS6, GDI2, GNAI2, GNB1, GPI, GPNMB, GSTO1, H3-3A, H3C15, H3F3B, H4C1, HCLS1, HNRNPA2B1, HNRNPD, HNRNPK, HP, HSP90AB1, HSP90B1, HSPA9, IGA2HC, IGGLC, IGH@, IKG, IGL@, IQGAP1, ITGB1, KCTD12, KRT1, KRT10, KRT9, LAMP1, LDHB, LPA, LRP1, MARCKS, MPO, MYH10, MYH11, MYH9, MYL12A, NPM1, ORM2, PDIA3, PDIA6, PFN1, PGAM1, PGK1, PLEC, PLS3, POSTN, PPIB, PRDX2, PRDX6, PRKCSH, PROS1, RAP1B, RPLP2, S100A11, S100A6, SAA1, SAMHD1, scFv, SERBP1, SERPINA10, SERPINA3, SERPINF1, SERPINH1, SH3BGR1, SOD3, SPP2, STOM, TALDO1, TF, TGM2, TKT, TLN1, TPI1, TPM3, TPP1, TUBB4B, UBA52, VCL, VCP, WDR1, YWHAE, YWHAG, YWHAQ, YWHAZ

Atherosclerosis proteins identified with differences in relative abundance (LFQ) and structural modifications (PLF)

A2M, ACTG1, ACTN4, AOC3, APOA1, APOA4, APOB, APOD, APOE, APOL1, APOM, AQP1, C3, C4A, C4BPB, C6, C8B, C8G, CALD1, CAVIN1, CDH13, CLIC1, CNN1, CNN3, COL18A1, COL4A1, CP, CRIP2, CTSB, CYB5R3, DEFA3, EFEMP1, EMILIN1, F2, FBLN1, FBLN2, FBLN5, FCN3, FERMT3, FGG, FHL1, FLNA, FMOD, FTH1, HBB, HPR, HSPG2, IGFALS, IGHG3, ILK, ITGB2, KLKB1, LAMC1, LASP1, LBP, LTBP1, LTBP2, LTF, MMP12, MMP9, NID1, OGN, PDIA4, PDLIM3, PGD, PGLYRP2, PLD3, PLG, PLTP, PON1, PZP, RTN4, S100A8, SAA4, SEPTIN7, SERPINA1, SERPINA4, SERPIND1, SERPINE2, SERPINF2, SERPING1, SLC2A1, SLC4A1, SOD1, SPTA1, SPTAN1, SPTB, TIMP1, TNXB, VTN

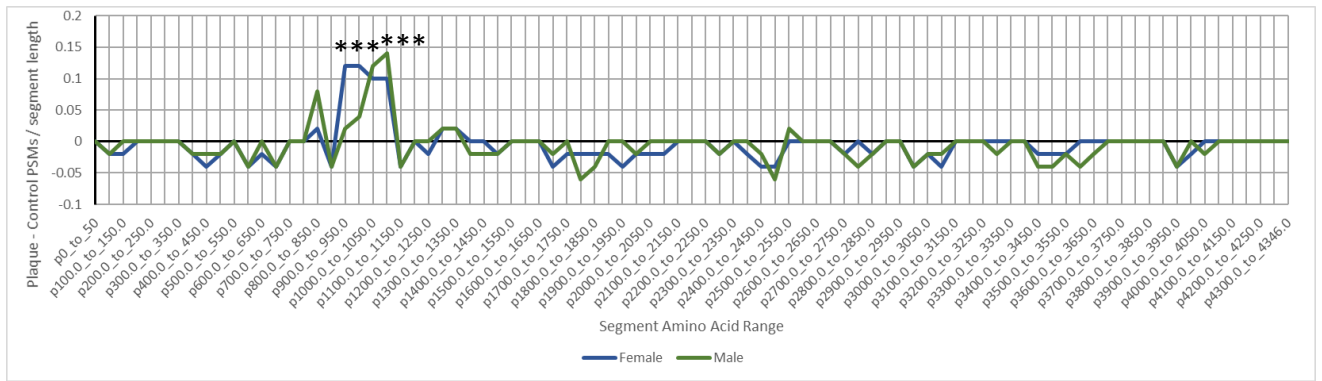


Atherosclerosis proteins identified with differences in whole protein relative abundance by LFQ

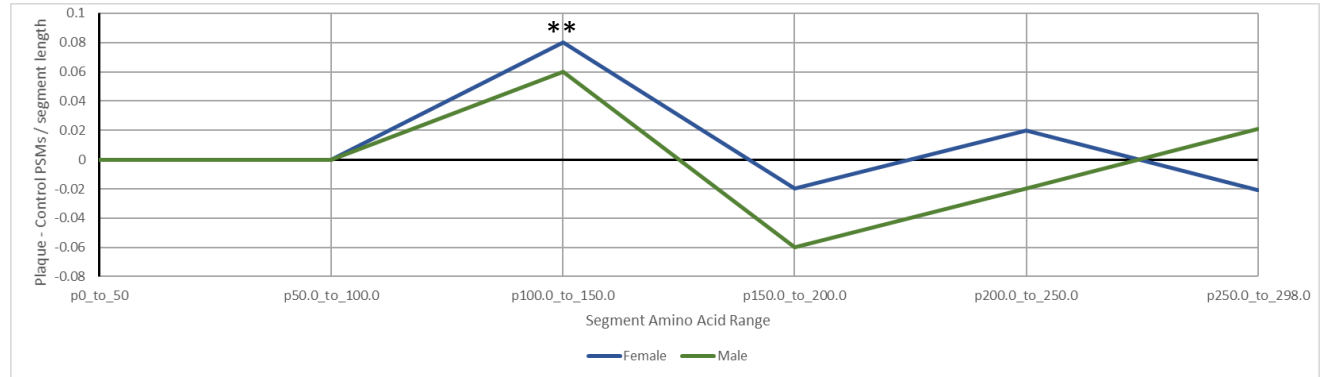
ABI3BP, ACAN, ACTA2, ADH5, ALCAM, ALDH1B1, ANXA3, APOC1, ARPC4, ARPC5, ATP6V1B2, AZU1, BCAM, C4B_2, C4BPA, C5, C8A, C9, CACNA2D1, CALU, CAMP, CAPN2, CAV1, CAVIN3, CD14, CD151, CD5L, CEMIP, CHMP4B, CKAP4, CMPK1, CNN2, CPB2, CRIP1, CRYAB, CSRP2, CTTN, DES, EHD2, ELANE, EPB42, ESYT1, FBLIM1, FCGBP, FERMT2, FGB, FTL, G6PD, GDI1, GLUL, GPLD1, GSN, HAPLN1, HAPLN3, HBA2, HBD, HDGF, HK3, HMCN1, HMGB1, HRG, HSPA2, HSPB1, HSPB6, IGFBP7, IGHA1, IGHA2, IGHG1, IGHM, IGHV3-23, IGKC, IGKV2D-28, IGLL5, ITGA1, ITGA3, ITGA8, ITIH2, ITIH4, ITIH5, JCHAIN, KNG1, KRT18, KRT8, LAMA5, LAMB2, LGALS1, LMCD1, LMNA, LMOD1, LOXL1, LPP, LTBP4, LYZ, MAP1B, MCAM, MFGE8, MMP1, MNDA, MXRA7, MYL3, MYL6, MYL9, MYLK, NAP1L4, NAPA, NEXN, NIBAN1, NID2, NT5E, NUCB1, PALLD, PARVA, PDLIM5, PDLIM7, PEBP1, PGM5, PRELP, PTGIS, QSOX1, RAN, RCN3, RNASE1, RNASE3, RRAS, RSU1, S100A12, S100A4, S100A9, SBSPON, SEPTIN2, SLC2A3, SLMAP, SMTN, SORBS1, SORBS2, SPARCL1, SPP1, SUN2, SYNPO2, TAGLN, TES, TGFB1I1, TIMP3, TINAGL1, TMSB4X, TNS1, TPM1, TPM4, TTR, VIM, ZYX

Figure S13. Protein targets of arterial atherosclerosis identified in the original Ward *et al.* (2018) study by label-free quantification (LFQ) of relative protein abundance and in this study by peptide location fingerprinting (PLF). PLF identified 152 proteins that were potentially unique to the approach, with plaque-associated significant differences in protein structure but not abundance.

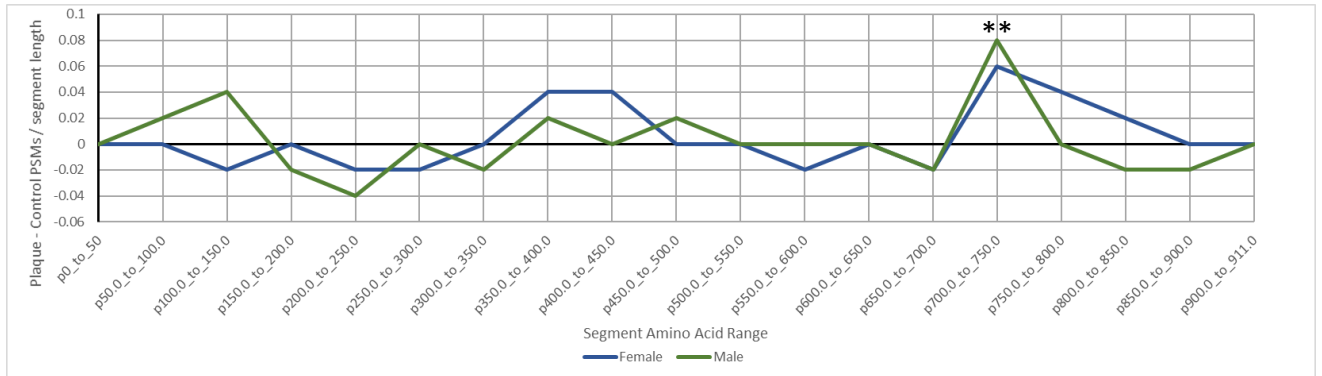
Heparan sulfate proteoglycan 2 (Perlecan; HSPG2)



Mimcan (OGN)



Alpha-actinin-4 (ACTN4)



Apolipoprotein B (APOB)

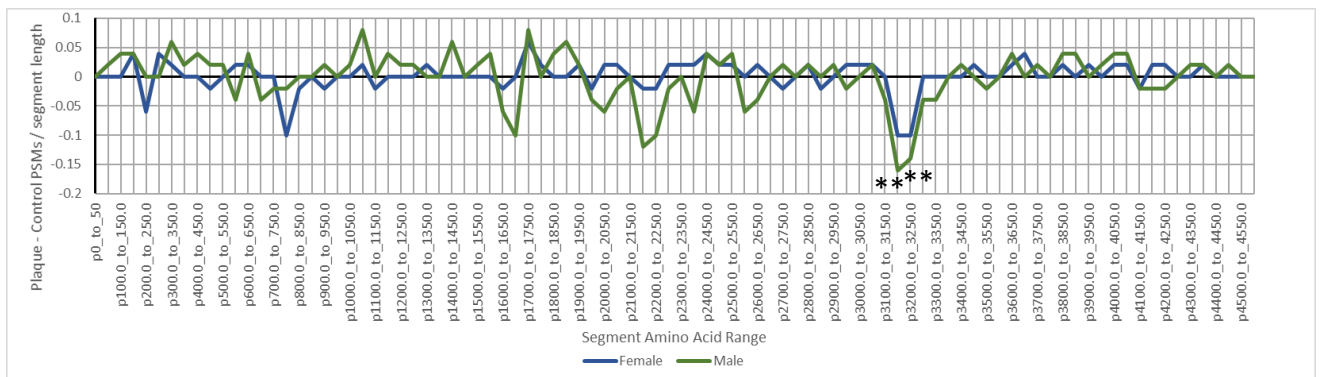
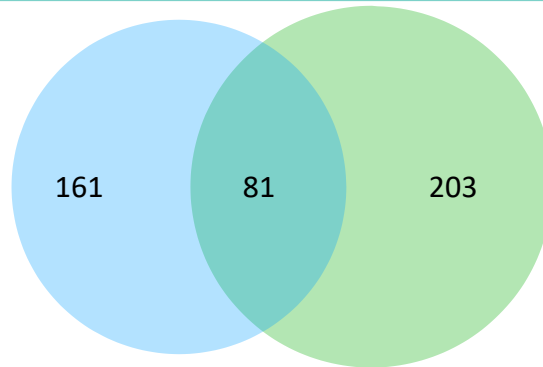


Figure S14. Non-normalised representations of composite lines graphs (**Fig. 10**) of proteins displaying sex-conserved, significant differences in peptide yield across their segmented structures between plaque and control artery ($y = 0$ indicates either no difference between plaque and control or missing values in both groups; stats = paired Bonferroni-corrected, repeated measures ANOVAs: *, $p \leq 0.05$; **, $p \leq 0.01$; ***, $p \leq 0.001$; stars = significant in both female and male).

Shared Biomarker Candidates between Ageing (IVD) and Age-dependent Atherosclerosis (Artery)

A2M, ACTB, ACTG1, ACTN4, AHNAK, AMBP, APOA4, APOB, APOE, C2, C3, C4A, C6, CALD1, CAST, CAVIN1, CDH13, CLEC3B, COL14A1, COL1A1, COL1A2, COL4A1, COL4A2, COL5A1, COL6A1, COL6A2, CYB5R3, DPYSL2, EEF1A1, F13A1, F2, FBLN1, FBLN2, FHL1, FLNA, FN1, GDI2, H4C1, HP, HSP90AB1, HSPG2, ITGB1, KRT1, KRT10, KRT9, LAMC1, LRP1, LTBP2, MPO, MYH10, MYH11, NID1, ORM2, PDIA6, PFN1, PGD, PLEC, PLG, PLS3, PRDX2, PRKCSH, RAP1B, SERPINA1, SERPINA3, SERPINA4, SERPIND1, SERPING1, SLC4A1, SOD3, SPTA1, SPTAN1, TALDO1, TF, TGM2, THBS1, TIMP1, TNC, TNXB, TUBB4B, VCAN, VTN



Atherosclerotic Artery-only Biomarker Candidates

ACTC1, ACTR2, ACTR3, AEBP1, AFM, ALB, ALDH2, ANK1, ANPEP, ANXA1, AOC3, APOA1, APOD, APOL1, APOM, AQP1, ARPC3, ASAH1, ATP5F1B, ATP6V1A, C1QA, C1QB, C1R, C4BPB, C7, C8B, C8G, CALR, CANX, CAPG, CAPZB, CCT5, CD36, CFHR1, CFI, CFL1, CLIC1, CLU, CNDP2, CNN1, CNN3, COL12A1, COL18A1, COL3A1, COL8A2, CORO1A, CP, CPN2, CRIP2, CSPG2, CSRP1, CTSB, CTSZ, DEFA1, DEFA3, DPYSL3, DSTN, EEF2, EFEMP1, EIF4A1, EMILIN1, EMILIN2, F10, FBLN5, FCN3, FERMT3, FGG, FMOD, FTH1, GAS6, GNAI2, GNB1, GPI, GPNMB, GSTO1, H3-3A, H3C15, H3F3B, HBB, HCLS1, HNRNPA2B1, HNRNPD, HNRNPK, HPR, HSP90B1, HSPA9, IGA2HC, IGFALS, IGGC, IGH@, IGHG3, IGK, IGL@, ILK, IQGAP1, ITGB2, KCTD12, KLKB1, LAMP1, LASP1, LBP, LDHB, LPA, LTBP1, LTF, MARCKS, MMP12, MMP9, MYH9, MYL12A, NPM1, OGN, PDIA3, PDIA4, PDLIM3, PGAM1, PGK1, PGLYRP2, PLD3, PLTP, PON1, POSTN, PPIB, PRDX6, PROS1, PZP, RPLP2, RTN4, S100A11, S100A6, S100A8, SAA1, SAA4, SAMHD1, scFv, SEPTIN7, SERBP1, SERPINA10, SERPINE2, SERPINF1, SERPINF2, SERPINH1, SH3BGRL3, SLC2A1, SOD1, SPP2, SPTB, STOM, TKT, TLN1, TPI1, TPM3, TPP1, UBA52, VCL, VCP, WDR1, YWHAE, YWHAG, YWHAQ, YWHAZ

Ageing IVD OAF-only Biomarker Candidates

A1BG, ABI3BP, ACAN, ACLY, ACO2, ACTN3, ANGPTL2, ANGPTL5, ANXA2, ANXA5, ANXA7, APCS, ARF1, ARF3, ARHGDI, ARPC4, ATP1A1, BGN, C1S, CA2, CALM1, CALM2, CALM3, CALU, CAPS, CAVIN3, CCDC80, CCN2, CD109, CDH1, CFH, CHAD, CHRDL2, CILP, CILP2, CKM, CLEC3A, CLTC, COL11A1, COL11A2, COL15A1, COL2A1, COL5A2, COL6A3, COL8A1, COL9A1, COL9A2, COL9A3, COMP, CPNE3, CPXM2, CRYAB, CSPG4, CTGF, CTSG, DAG1, DDOST, DKK3, DPT, DRIP4, DYNC1H1, ECM1, ECM2, EEF1A1P5, EEF1G, EMILIN3, ENO3, ENPP1, ENPP2, ERP44, FBN1, FBXO2, FGA, FGB, FLNB, FLNC, FNDC1, FRZB, FSCN1, FTL, GAA, GANAB, GAPDH, GBE1, GC, GCS1, GLUD1, GSN, GSTP1, H1-0, H1-5, H2BC11, H2BC21, H2BC3, HBA1, HBD, HEL-214, HEXA, HHIPL2, HIST1H1E, HNRNPH1, HNRNPU, HPX, HRG, HSPA1A, HSPA1B, HSPA5, HSPA8, HTRA1, HTRA3, IDH2, IGFBP3, IGFBP7, IGHM, IGK@, IGLC1, ISLR, ITGAV, ITIH1, ITIH2, ITIH4, ITIH6, KNG1, KRT19, LAMA2, LAMA5, LAMB1, LAMB2, LCP1, LGALS3BP, LOXL3, LRG1, LTA4H, MAP1B, MATN2, MDH2, MELTF, MRC2, MSN, MXRA5, MYOM2, NACA, NCL, NEB, NID2, NNMT, NUCB1, NUCB2, OAF, OLFML1, P4HA1, PAM, PCOLCE2, PDCD6IP, PDGFC, PEBP1, PLOD1, PPIC, PRDX3, PRDX4, PRG4, PRKAR1A, PRTN3, PSAP, PSMA7, PTRF, PXYLP1, PYGL, PYGM, RACK1, RBMX, RPN1, RPN2, S100A9, SCIN, SEMA3C, SEMA3E, SERPINB6, SERPINE1, SET, SMOC1, SMOC2, SNC73, SPARC, SRI, SRPX2, STRF8, SYNCRI, THBS2, THBS3, THBS4, TIMP3, TINAGL1, TPM1, TTR, TUBA1A, TUBA1B, TUBB, TUBB2C, TXNDC5, UGDH, VASN, VWA1

Figure S15. Shortlisted protein targets of human IVD ageing and arterial atherosclerosis identified with structure-associated differences by peptide location fingerprinting (PLF). PLF identified 81 proteins which were affected by ageing and in this age-related disease.